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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
JIANG, DONG

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 02/13/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/578,063	MCCARTHY ET AL.	
	Examiner	Art Unit	
	Dong Jiang	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 January 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-10 and 24-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-10 and 24-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *8-10 and 24-46* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED OFFICE ACTION

Applicant's election without traverse of Invention B, claims 8-10, in Paper No. 9 is acknowledged. Applicant's sequence election with traverse of SEQ ID NO:47 in Paper No. 9 is acknowledged. The traversal is on the ground(s) that each of SEQ ID NOs:48-52 is a portion of SEQ ID NO:47, and each of SEQ ID NOs:45 and 46 encodes SEQ ID NO:47, therefore, the search relating to SEQ ID NO:47 will necessarily include searches of each of SEQ ID NO:45, 46, and 48-52. In view of the relationship of SEQ ID NOs:45-52, the Examiner decides to join SEQ ID NOs:45, 46, 49 and ATCC207220 with SEQ ID NO:47 for examination, as they are the polynucleotide encoding the polypeptide of SEQ ID NO:47, and the mature form of SEQ ID NO:47. However, it is not found persuasive that a search of SEQ ID NO:47 will necessarily include searches of each of SEQ ID NO:48-52 because a small portion of a disclosed polypeptide, such as SEQ ID NO:48 or 51, requires a separate search of the databases. Due to the use of 'comprising' language, it cannot even be said that the search for amino acids 1-423 of SEQ ID NO:47 would reveal art pertaining to, for instance a polypeptide *comprising* a region encoding amino acids 255-279 of SEQ ID NO:47 (as SEQ ID NO:51), as the latter could be found embedded in a completely different protein. Accordingly, the restriction is still deemed proper and is therefore made FINAL. SEQ ID NOs: 48 and 50-52 are withdrawn from further consideration as being drawn to a non-elected invention.

Applicant's preliminary amendment in paper No. 9 is acknowledged and entered. Following the amendment, the original claims 1-7 and 11-23 are canceled, claims 8 and 9 are amended, and the new claims 24-46 are added.

Currently claims 8-10, and 24-46 are pending and under consideration. The claims will be examined to the extent that they read on SEQ ID NOs:45-47 and 49.

Formal Matters:

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because: the first two inventors did not sign their name in full.

Claims 8, 9, 24, 30, and 44 are objected to for encompassing a non-elected subject matter, SEQ ID NO:48, and 50-52. The applicant is required to amend the claims to read only upon the elected invention.

Objections and Rejections under 35 U.S.C. §101 and §112:

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 8-10, and 24-46 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by a credible, substantial, specific, or well-established utility.

Claims 8-10, and 24-46 are directed to an isolated human polypeptide sequence of SEQ ID NOs:47 and 49 encoded by nucleic acids of SEQ ID NO:45 or 46, variants and fragments thereof, and pharmaceutical composition thereof. Said polypeptide is designated TANGO294.

The specification asserts that TANGO294 protein is involved in facilitating absorption and metabolism of fat, thus, can be used to prevent, diagnose, and treat disorders involving one or more physiological activities mediated by TANGO294 protein. Such disorders include, for example, inadequate expression of gastric/pancreatic lipase, cystic fibrosis, exocrine pancreatic insufficiency, fat malabsorption, obesity, and the like (page 8, the last paragraph, and page 76, line 26 to page 77, line 2).

The asserted utilities discussed above are not considered to be credible because such assertion is based on that human TANGO294 protein exhibits considerable sequence similarity to lingual and gastric lipase proteins of rat, dog, and human (page 75, lines 17-21). As stated in the specification, the sequence similarity of TANGO294 and mammalian lingual, gastric, and lysosomal acid lipase proteins indicates that TANGO294 is involved in facilitating absorption and metabolism of fat (page 76, lines 23-25). Such prediction based upon sequence similarity of known proteins is not credible, and cannot be accepted in the absence of supporting evidence, because it is well known that many proteins belong to a same family, share a high degree of

sequence similarity, yet have diverse, and sometimes even opposite biological activities and functions. For example, in the transforming growth factor (TGF) family, Vukicevic et al. (1996, PNAS USA 93:9021-9026) disclose that OP-1, a member of the TGF-family of proteins, has the ability to induce metanephrogenesis, whereas closely related TGF- family members BMP-2 and TGF-1 had no effect on metanephrogenesis under identical conditions (p. 9023, paragraph bridging columns 1-2). Additionally, Skolnick et al. (Trends in Biotechnology, 2000) teaches that because proteins can have similar structures but different functions, determining the structure of a protein may not necessarily reveal its function (see entire article, especially Box 2). Brenner (1999, Trends in Genetics 15:132-133) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, then most homologues must have different molecular and cellular functions. Therefore, in the absence of any actual experimental confirmation of any of biological properties, the skilled artisan would not accept the asserted activity as being credible, even though the assertion that TANGO294 may be a lingual, gastric lipase, and involved in facilitating absorption and metabolism of fat is specific, and substantial.

Therefore, each of the disclosed utilities requires additional knowledge about the claimed nucleic acids and the protein encoded thereby before the nucleic acids or protein can be used for a specific purpose, such as those set forth in the specification. The specification does not provide any of such specific information about SEQ ID NO:45, 46, or 47. The disclosed uses in diagnosis, drug development, and treatment are not credible, in the absence of knowledge of the substrate which said TANGO294 bind, any disclosed gene mutation, or any disease or condition which could be so diagnosed, or treated. Therefore, there is no immediately available patentable utility for TANGO294 or nucleic acids encoding such. Upon further research, a credible utility might be found for the claimed isolated polypeptide. This further characterization, however, is part of the act of invention, and until it has been undertaken, the claimed invention is incomplete.

The instant situation is analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-tumor activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its

broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately apparent or fully disclosed "real world" utility. The court held that:

> The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field. ... a patent is not a hunting license. ... [i]t is not a reward for the search, but compensation for its successful conclusion.

The instant claims are drawn to a polypeptide of as yet undetermined function or biological significance. There is no evidence of record or any line of reasoning that would support a conclusion that the claimed TANGO294 was, as of the filing date, useful for diagnosis and treatment of any of disorders as stated in the paragraph bridging pages 76 and 77 in the specification. Until some actual and specific biological significance can be attributed to the polypeptide identified in the specification as TANGO294, one of ordinary skill in the art would be required to perform additional experimentation in order to determine how to use the claimed invention. Thus, there was no immediately apparent or "real world" utility and the claimed invention is incomplete as of the filing date.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8-10, and 24-46 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Further, even if the specification taught how to use human TANGO294, enablement would not be commensurate in scope with claims 8, 42, 46, and the dependent claims 10, and 24-

39, and 43-45, which encompass fragments of SEQ ID NO:47 (claims 8, 24-27, for example), % variants of the fragments (claim 42 and 46, for example), allelic variants of SEQ ID NO:47 (claims 8 and 30, for example), hybridization variants (claims 30 and 31), and % variants (claims 35-39, for example).

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with the claims. The specification discloses merely *one* human TANGO294 with SEQ ID NO:47 and the nucleic acids encoding such with SEQ ID NO:45 and 46, respectively. No other TANGO294 variants or fragments meeting the limitations of these claims were ever identified or particularly described. The specification provides neither guidance, nor working example to teach how to make any of variants or fragments of TANGO294. Since a biological function of TANGO294 is not disclosed in the specification, and since one skilled in the art could not determine with a reasonable expectation of success what a biological function of TANGO294 would be, the skilled artisan would not be able to make TANGO294 variants or fragments, and test them for a biological activity, because one is not disclosed. Furthermore, the specification provides no guidance as to how the skilled artisan could use an inactive TANGO294 variant or fragment, as *no functional limitation* associated with the TANGO294 variants or fragments in the claims (claims 8, 24, and 30, for example). Therefore, it would require undue experimentation to practice this invention as claimed, because the skilled artisan would have no reasonable expectation of being able to use the TANGO294 variants or fragments for any purpose stated in the specification. With respect to the hybridization variants, it is well known in the art that hybridization will occur even under highly stringent conditions if there is only local identity between two molecules whose sequences might be totally divergent outside of that region, and hybridization would be expected to occur under low stringent conditions if two molecules share only certain degree of sequence homology. Such hybridized molecules may encode proteins having distinct biological functions from those of the SEQ ID NO:47. Therefore, it would require undue experimentation in order to use the claimed invention in its full scope. Further, as there is not functional limitation associated with the polypeptides encoded by the claimed polynucleotides, the specification has not taught a skilled artisan how

to use the polypeptides encoded by the hybridization variants, and not sharing functional properties with TANGO294.

Furthermore, even if there were utility and enablement of a protein having SEQ ID NO:47, claims 8 and 30 would be further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claim limitation in claim 8, part b), and claim 30 is directed to a naturally occurring allelic variant of SEQ ID NO:47. The specification discloses the polypeptide of SEQ ID NO:47. No other variants of SEQ ID NO:47 meeting the limitations of these claims were ever identified or particularly described. The skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8-10 and 24-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 8 is incomplete for omitting essential elements. Part b) of the claim is limited by a hybridization method under stringency conditions. The specification does not define such conditions. As the target sequence is specific, an artisan needs to know the specific corresponding hybridization conditions in order to practice the claimed invention. The claim recites neither hybridization conditions to ensure that any hybridized polynucleotides will

comprise specific sequence within the meaning of the disclosure, nor process steps which would effect the removal of nonspecific hybridization complexes. Without knowing what conditions are comprised by "high stringency" conditions, one can not determine the metes and bounds of nucleic acids within the limitations of the claim.

Claim 30 is similarly indefinite.

Claim 31 is incomplete for omitting essential elements. It is not clear how long the washing step is carried out, which is critical for the removal of nonspecific hybridization complexes.

Claim 8 is further indefinite for the recitation of "*either* of SEQ ID NO:47 *and* amino acid sequence" in part a), lines 3-4. It is suggested to substitute with "either ... or ...". It is also suggested that the word "and" in "SEQ ID NO:45 *and* 46" in line 5 is replaced by a comma.

Claim 8 is further indefinite for the recitation of "*a portion* which ..." in part c), line 1. It is unclear how much is "*a portion*", whether *"a portion"* requires any biological activity, and whether it is fused to a lipase. Therefore, the metes and bounds of the claim cannot be unambiguously determined.

Claims 42 and 43 are similarly indefinite.

Claim 8 is further indefinite for the recitation of "*any of* SEQ ID NOs:47-52 *and* the amino acid sequence ..." in lines 1-2 of part a), and line 4 of part c). "Any *one* of SEQ ID NOs:47-52, the amino acid sequence ..." is suggested. Similar recitation is present in multiple claims, claims 9, 24, 30, for example, corrections are required for all claims containing such recitation.

Claims 9 and 35 are indefinite for the recitation of "a complement thereof. As the claims are directed to an isolated polypeptide, it can not be encoded by the complement strand of the cDNA encoding the polypeptide.

The remaining claims are rejected for depending from an indefinite claim.

Prior Art:

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Anderson et al. (J. Biol. Chem., 266:22479-84, 1991) discloses an amino acid sequence of a human lysosomal acid lipase (Figure 4) comprising residues 15-409 of SEQ ID NO:47 of the instant application with 61% homology, and a polynucleotide encoding the same with 83.2% sequence similarity to a polynucleotide encoding amino acid residues 2-409 of SEQ ID NO:47 of the present invention (see computer printout of the search results).

Du et al. (Locus HSU08464, GenEmbl, 1994) teaches a polynucleotide sequence of a human lysosomal acid lipase, which comprises nucleic acid residues 39-1241 of SEQ ID NO:46 of the instant case with 65.4% homology (see computer printout of the search results).

Conclusion:

No claim is allowed.

Advisory Information:

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 703-305-1345. The examiner can normally be reached on Monday - Friday from 9:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is 703-308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

DJ
2/6/02